ABSTRACT

Background Observational research is increasingly important in clinical decision-making. Opt-out consent has been proposed as a more practical way to obtain participants' consent for such. We evaluated patients' views on opt-out consent for observational research by identifying perceived benefits and barriers.

Methods Following a systematic literature review of research on participants' perspectives on opt-out consent, we conducted a focus group interview with oncological patients and their family members.

Results We identified thirteen articles detailing perspectives on opt-out consent. Perceived advantages included benefitting medicine and future generations. These findings were confirmed in our focus group. The main reported barriers to opt-out consent are concerns regarding privacy and the sharing of data with third parties. Participants also demonstrated concerns on insufficient education on opt-out consent.

Conclusions Participants demonstrated willingness to participate in observational studies utilizing opt-out consent. Special focus should be placed on outlining existing safeguards in research.

Key points

- Our results include a comprehensive systematic review of the literature following the PRISMA guidelines.
- Additional qualitative data was obtained from a focus group, an experienced research consumer panel, and an existing real world evidence database.
- Participants demonstrated willingness to participate in studies utilizing opt-out consent, however this was impeded by some key concerns.
- Special focus should be placed on outlining the existing safeguards in research.
- Improving public opinion on studies using presupposed consent could lead to decreased selection bias.
- Nonetheless, the scope for opt-out consent has been further limited by the provisions of the General Data Protection Regulation (GDPR) which came into force in May 2018.

Reflective questions

- How do patients perceive an opt-out consent procedure?
- What are current barriers for patients to approve of opt-out consent?
- How does the interpretation of the General Data Protection Regulation affect the use of opt-out consent in academic research?

INTRODUCTION

The significance of providing personalized care to patients is increasingly recognised in current medical practice. An invaluable tool to this purpose is *real-world evidence* (RWE). RWE refers to data, mostly observational, collected in contexts other than typical research settings, such as during routine clinical care.(1, 2) Unlike other forms of data collection, including randomised controlled trials, RWE has greater external validity and better applicability to underrepresented patient groups due to decreased selection bias.(1, 3-5) Hence, the use of RWE is permissive to clinicians more equitably addressing the needs of singular patients in real-world, day-to-day contexts.

Yet maintaining the benefits of RWE can be challenging, as much validity can be lost whilst obtaining participants' consent. Selection bias is bound to occur when participant consent is secured via the currently widespread opt-in recruitment strategy, as has been demonstrated in various studies.(6-9) It can be argued, however, that when the collection of observational RWE poses remote risks of harm to the participants involved, opt-out consent can be utilised.(10-12)

Opt-out systems rely on implicit consent, where willingness to participate is tacit or presumed and can be retracted by active objection.(13) These generate more complete data, with less biased samples and improved response rates, as compared to opt-in consent strategies.(9, 14, 15) Moreover, opt-out consent is preferable in large cohorts, where other strategies could be too costly or impractical to enact.(12, 16-18) However, it is unclear whether public opinion unequivocally supports opt-out. Existing studies demonstrate the public holds varying views about which process of consent is ideal.

Hence, the aim of this study was to explore cancer patients' opinions of opt-out consent for the secondary use of their health records. Following a systematic review of the literature, we conducted a focus group with oncological patients and their relatives, furtherly exploring their

opinions and concerns. In addition, we assessed the experience of opt-out consent in real-time clinical practice in our institution.

METHODS

Systematic literature review

This systematic review was conducted following the PRISMA statement for completing systematic reviews and meta-analyses (19). A computerised literature search of the Ovid MEDLINE database to identify full text and abstracts published between 1946 and November 21st 2017 was performed. The following search strategy was used: Opt-out and (consent or view* or perspective* or ethic* or attitude*) and (research or biobank or trial or health record* or medical record*). All references of the selected articles were checked, including hand searches.

The final articles were chosen based on the following set of inclusion criteria: the publication pertained to a patient-focused study which clearly defined opt-out; the manuscript was published in English. The literature review and data collection was conducted by LC and reviewed by MVH.

Initially, titles were reviewed to assess whether they met inclusion criteria. Titles that indicated the study met these criteria progressed to an abstract review. Upon inclusion after this step, the full manuscript was thoroughly checked to evaluate inclusion and exclusion criteria. Figure 1 provides more detailed information regarding the exclusion process. The following details were recorded for each study: author, year of publication, country where study was undertaken, number of participants, and method of data collection.

Focus group participants and setting

Patients being treated at Guy's Cancer Centre (London, UK) for urological tumours, breast or lung tumours were recruited to participate in a focus group by invitational flyers handed out

whilst visiting the Centre for routine appointments. Family members and relatives were also encouraged to participate. We aimed to have at least 10 participants as to ensure all relevant themes and opinions would be picked up (20). Participants were introduced to the purpose of the focus group and asked to complete an anonymous demographic questionnaire. Informed consent was obtained for the recording and processing of the interview. The focus group was conducted by a research nurse and two note-taking assistants. Initially, broad questions about participants' previous exposure to research were discussed. Subsequently, a brief presentation on selection bias and opt-out research with secondary use of medical records was held. This presentation illustrated: 1) the mechanism of opt-in consent; 2) how selection bias can arise; 3) the mechanism of opt-out consent; 4) the advantages and disadvantages of opt-out consent, as compared to opt-in. Participants were asked to illustrate their reactions to an opt-out consent methodology, discussing the favourable aspects of such and their concerns. The discussion was framed on a set of questions developed on the common themes identified in the literature review (Table 1), however participants were encouraged to voice any other relevant ideas and free discussion amongst the group was supported.

Further validation for the focus group findings was also sought from the South East London Consumer Research Panel on Cancer (SELCRP). This is a group of patients, patient advocates and researcher representatives providing advice to researchers on study proposals and other topical issues. The SELCRP received the same brief presentation on selection bias and opt-out research as the focus group. Subsequently, representatives were encouraged to voice their views on presupposed consent for medical research.

Data analysis

The focus group was fully audio recorded and transcribed verbatim. The resulting transcript was analysed thematically, coding topics mentioned with the NVivo 11 software (QRS international, 2017).(21) Emergent themes were identified and grouped into broader statements, which were furtherly elucidated in view of the literature review findings.

Institutional experience of opt-out consent

Consecutive patients entering an ethically approved opt-out clinical database for patients with cancer of the upper gastro-intestinal tract at our institution were observed over a one year period for tolerability and withdrawal of consent (REC 17/NW/0377). Information regarding the use of data, access to data and the process for opting-out was made available to all patients as standard.

Patient and Public Involvement

As outlined above, patients and public were at the centre of this work. The study aimed to identify how opt-out can be used in future to conduct studies based on anonymised, routinely collected data. We worked with our patient support groups to identify relevant research questions and themes and also involved them in our interpretation of the findings from the systematic literature review. Hence, we have full PPI support for the findings and write-up of the current manuscript. The published manuscript will be shared with the wider patient support network at our hospital.

RESULTS

Literature review

The PRISMA flow diagram in Figure 1 shows the 367 unique hits yielded from our search. Titles and abstracts were screened. Twenty-nine titles meeting the criteria were reviewed in their full text by two authors. Additional relevant studies were identified hand searching bibliographies and utilising the "similar articles" function in PubMed. The resulting 13 papers included 5 studies focussing on opt-out consent for the institution of biobanks,(22-26) whilst 8 addressed opt-out consent for the secondary use of medical records.(27-34)

Characteristics of included studies are collated in Table 2. Common themes identified in the literature review were subdivided into statements of support versus concern on opt-out consent, and are summarised in Tables 3 and 4. As this review included qualitative studies, a quantitative synthesis was not performed.

Support of an opt-out consent strategy

Ten of the thirteen studies included in this review specifically reported participants supporting opt-out consent, acknowledging its importance in progressing medical knowledge.(22, 25-32, 34) Other rationales for support included providing benefit to others, to self or family and to other patients with the same disease.(22, 24)

Seven studies noted participants support opt-out consent specifically because of their trust in researchers or in the research institution.(22-24, 28, 30-32) In such cases, participants were confident the sensitive data collected from opt-out studies would be effectively protected.

Participants recognised the convenience of opt-out consent, both from the viewpoint of study subjects and of the organising researchers. In one paper, participants preferred opt-out over other forms of consent, as it eliminates the need for redundant consenting for repeated studies.(25) From researchers' perspectives, three studies recognised that opt-out systems are more cost- and time- effective than other forms of consent, thus facilitating research.(25-27)

Participants stated that presupposing consent is acceptable as long as certain safeguards are present. Centrally, participants accepted opt-out systems insofar as the choice of opting-out is clear, and possible at all times.(23, 25, 27, 33) This was argued to allow free judgement, whilst providing flexibility for subjects changing opinion throughout the study. Also, participants requested the anonymisation of their personal data.(23, 30, 32) Two studies reported desire for the provision of an independent review group functioning as a "watchdog" protecting subjects' interests.(27, 33)

Concerns about an opt-out consent strategy

The key concerns on opt-out consent reported by the literature regard privacy and its protection. Participants were troubled that presupposing consent could entail loss of privacy, especially due to possible breaches in confidentiality.(22, 24, 26-33) Moreover, three papers reported scepticism on the security measures present to protect the confidential data collected.(30, 31, 33)

Studies recorded adversity towards third parties' use of data from opt-out research. Participants disapproved of commercial data sharing, being concerned by use of data for purposes other than benefitting patients and by third parties' privacy policies.(28, 32, 33) Participants were also concerned with inappropriate use of data by parties such as banks, mortgage and insurance companies.(26, 27, 31-34) Studies reported concerns that inappropriate use of collected data could trigger discrimination of particular ethnic and religious groups.(30, 31, 33)

Finally, the literature registered apprehension on insufficient information being provided to research participants. Nine papers reported concern for inadequate details given prior to formulating consent, especially regarding the purpose of the research performed and on who is granted access to patients' data.(22, 26-29, 31-34) Concern for peers not reading or being able to

comprehend the information provided was also noted.(26, 29, 32, 33) Additionally, one study(29) reported worry on possible difficulties in indicating the will to opt-out, and one disapproved the passivity of the consent obtained in opt-out systems.(26)

Focus group

Thirteen patients and carers took part in our focus group. The demographics of participants are summarised in Table 5. Upon questioning, all participants had some understanding of medical research and its importance, most having either been approached for or taken part in research at least once. Nonetheless, prior to the presentation held, only one participant could explain what opt-out consent entails, reflecting that most of the public has been exposed to opt-in consent exclusively, due to its widespread use as the ethical gold standard in the healthcare context. Indeed, following the presentation many participants posed questions regarding the mechanisms of presupposed consent applied to secondary use of their records. When participants' understanding of opt-out consent was clarified, a broad support for it was registered (Table 6).

To facilitate analysis, participants' perceptions on opt-out consent were broadly categorised into statements of either support or of concern, with representative quotations reported in Table 7 and 8, respectively. Recurring themes were grouped to facilitate comparison with findings arising from the literature review.

Support of an opt-out consent strategy

Rationale for supporting opt-out research

The most cited reason for supporting opt-out consent was appreciation that research advances medical knowledge, fostering understanding of disease (Table 7). Participants

mentioned they would participate in an opt-out study to benefit future patients (Table 7). Improving practice for future generations, along with gratefulness to past research subjects, the hospital and the NHS, made presupposed consent in research acceptable to participants, who likened it to a form of public duty (Table 7).

Trust for researchers and research institutions

Upon probing, all participants agreed having great trust in the medical institution attended for treatment. Crucially, participants confided in researchers, hence would likely engage if an opt-out study were to be established (Table 7). Participants were certain their care standard would be unaltered in spite of any decision to opt-out from a future study (Table 7).

Safeguards- opportunity to opt-out

Participants were unambiguous that their participation in opt-out research would be dependent on the key condition it were clear they could opt-out, and at any moment (Table 7).

Harassing research requests

Discussing research in general, participants were fearful of being "bombarded" or harassed by researchers' recruitment requests. Participants were apprehensive researchers could insistently request participation or do so at inopportune moments, as had happened to many in the past (Table 7). Specific concern was voiced on receiving unsolicited phone calls and emails by researchers (Table 7). Participants felt reassured when explained that an opt-out observational study of their medical records would not entail getting contacted other than for initial opting-out, constituting a strong basis of preference for opt-out consent.

Concerns about an opt-out consent strategy

Data protection and privacy

Participants manifested worry for the loss of privacy that an opt-out consent system could entail, presupposing that data mishandling or corruption would be inevitable (Table 8). Whilst they agreed this would make them question their participation, not necessarily it would discourage them to opt-out.

Sharing information with pharmaceutical companies

Participants were apprehensive the data obtained from opt-out research could be shared with third parties, chiefly pharmaceutical companies. Concern was raised that these have questionable data handling methods and ineffective privacy policies (Table 8). However, participants also acknowledged the existence of a dilemma, constituted on one part by the scepticism of the public against pharmaceutical companies, and on the other by the benefits of conceding data to these, including monetary compensation supporting research and the chance of contributing to the development of new drugs (Table 8).

Inappropriate use of data by other third parties

Patient's scepticism on the sharing of opt-out research data with third parties extends to commercial entities other than the pharmaceutical industry, particularly mortgage and insurance companies. Participants recognised that if sensitive data were shared or leaked to these, discrimination towards particular groups could arise (Table 8).

Patients' comprehension of opt-out consent

As previously mentioned, most participants had no prior knowledge of opt-out consent, and concern was voiced that other patients might not comprehend the functioning of an opt-out system at first presentation. Allusions to the public's functional illiteracy were made, and concern was voiced on the understanding of at-risk groups of patients (Table 8). Participants underlined the need for clear and concise information throughout (Table 8). This would increase the likelihood that they read and understood the introductory statement to an opt-out study. Participants also suggested the use of descriptive illustrations, informative posters, text messages, and of digital media to elucidate opting-out (Table 8).

Desire for more information

Throughout the focus group, participants underlined the desire for additional information on how their data would be used and what research would be performed in an opt-out study. Many supported that explaining patients the usefulness of their data through anecdotes could provide them with greater incentives to participate in research, bolstering presupposed consent (Table 8).

Patient-consumer panel

The participants consulted as part of the patient-consumer panel reiterated and reinforced the focus group findings supporting opt-out systems. Similarly to the focus group held, particular emphasis was placed upon the need for detailed yet clear information given to prospective participants in research presupposing consent. The use of forms of communication alternative to simple text, including images, posters, and digital media, was discussed in detail and supported by participants.

Institutional experience of opt-out consent

Opt-out consent for collection of data by the designated clinical care team has been an integral part of data capture for patients with upper gastro-intestinal cancer in our institution for one year (35, 36). Combining ethical approval and support from a major patient representative body as part of the consultation process, more than 100 consecutive patients have been successfully enrolled within this system without any withdrawal of consent to date. Data is explicitly for use by the clinical team and transfer to third parties, including pharmaceuticals, is not permitted. Patient feedback has been extremely positive and many also choose to enrol in further research projects for which study-specific consent is obtained.

DISCUSSION

Combining the recurring themes from our focus group with our synthesis of existing literature and institutional experience reveals the public's willingness to participate in research recruiting on the basis of opt-out consent. This is motivated by the will to advance medical knowledge and to benefit future generations. A novel finding from the focus group discussion is support of opt-out recruitment as a form of public duty. This perception of opt-out consent accords with proposed theories that research should be regarded a moral imperative.(37, 38) Most importantly, it denotes underlying propensity of the public to join research, fundamental to the presupposed consent of opt-out systems.

Whilst the advantages of opt-out consent systems were recognised in some papers analysed, the literature and our focus group showed participants were generally unaware of such. Only one reviewed paper noted that opt-out consent can eliminate the necessity of repeated consents for singular studies.(25) This is particularly relevant considering the apprehension for

297 redundant recruitment requests uncovered during our focus group. From the researchers'
298 viewpoint, only three studies reported appreciation of opt-out systems' organisational, economic
299 and time effectiveness in respect to other consent methods.(25-27). Though discussed in the
300 introductory presentation, this was not recognized in our focus group, where only one participant
301 acknowledged the advantage of limiting selection bias. This reveals that effective education of the
302 public with regards to the benefits and conveniences of opt-out consent is essential for its
303 support.

304 Albeit focus group participants were supportive of opt-out systems, they were so at the
305 specific condition that opting-out is ensured possible, and at all times. This finding is echoed in
306 four papers included in the review.(23, 25, 27, 33) The request for this safeguard to autonomy
307 denotes the fundamentality of independent choice to participants.(23, 27, 30, 32, 33)
308 Notwithstanding these requests, focus group and literature participants failed to mention existing
309 safeguards currently present in medical research, including research ethics committees, NHS and
310 hospital governance protocols.(34, 39) This suggests participants' safeguarding requests to be
311 secondary to their unawareness of pre-existent protections, additionally implying the need for
312 greater education of the public. Overall, the trust avowed to researchers and institutions in the
313 literature and our focus group outlines the basis for support of opt-out research, however
314 elucidating present safeguards should provide further reassurance to participants, bolstering
315 support of opt-out. (22-24, 28, 30-32)

316 Two main concerns on opt-out consent were uncovered, many shared between the focus
317 group participants and the audited literature: (1) data protection and (2) third parties' use of data.
318 Firstly, participants presupposed that breaches in privacy are unavoidable, manifesting scepticism
319 on the security measures currently present – though better education about the process of data
320 anonymization should also better inform potential participants.(30, 31, 33) Secondly, participants

found the sharing of their data with commercial companies- chiefly the pharmaceutical industry- questionable, even though they could also identify benefits in terms of new drug development.(28, 32, 33) This delicate equilibrium underlying acceptability of commercial data sharing should be subject of future studies, elucidating the precise circumstances warranting approval by the public. With respect to use of data by companies such as banks, mortgage and insurance companies, it is crucial to inform participants that such sharing and use by third party companies is prohibited, both by data privacy legislation (including GDPR) and by the terms on which studies are authorised by ethical committees.

An overarching theme arising in both our focus group and the analysed literature is the necessity for additional public information regarding opt-out research. This finding was also confirmed by the discussion held in the patient-consumer panel consulted. Participants in our group and nine previous reports voiced concerns on receiving insufficient information regarding opt-out consent, tampering with their independent choice of participation.(22, 26-29, 31-34) Participants requested elucidations on the nature of the research performed and on the access to their data. Indeed, participants' unawareness of the benefits of presupposed consent and of the safeguards existent in research suggest that current public knowledge of opt-out research is inadequate. To promote the public's perception of opt-out consent, any information supplied should thus be easily accessible to all patient groups. Alternative forms of communication, including text messages and digital media such as videos, were also suggested by participants. Moreover, the strategic potential of publicity in gaining the approval of a wider public for opt-out recruitment systems should not be undervalued.

We made every effort to include all relevant publications available to date through various sources. In addition, clearly defined inclusion criteria were specified a priori. Nonetheless, our study is limited in that we only conducted one focus group comprised of oncological patients and

family. Due to the participants' background and recruitment by invitation, it is possible individuals highly engaged and favouring research were overrepresented. Moreover, some participants were previously acquainted with the research nurse conducting the group, possibly introducing response bias through social desirability. We tried to overcome these limitations by validating our findings consulting an experienced research consumer panel. No new views were identified through these discussions and hence we are confident that we reached a point of saturation (20). Our institutional experience of opt-out consent for use of data by clinical teams has also been very positive, affirming the principles outlined above in real world terms. However, it needs to be highlighted that all our qualitative work has focused on those affected by cancer and it is possible that this may influence their attitude in terms of health and research. Future studies should be done in other chronic disease settings.

The findings of this study should also be considered in light of the recent changes to data privacy laws in Europe. Of the papers reviewed, those performed in the UK were carried out at a time when the Data Protection Act 1998 was the applicable law, whilst the Canadian study falls under Canadian data protection laws, recognised by the EU as having general equivalence of effect to European Data Protection law and providing an adequate degree of protection. The American studies are subject to a data protection legislative framework generally less stringent than the former two. Nonetheless, all three systems allow- or allowed- valid consent to be given by opt-out methods.

The legal acceptability of opt-out as valid consent for processing personal data has changed substantially in Europe with the General Data Protection Regulation (GDPR) coming into force in May 2018.(40) Overall, GDPR raised the standard for consent, generally deeming opt-out to be no longer sufficient in showing valid consent for processing personal data. Rather, GDPR

requires consent to be explicit, freely given, specific, informed and unambiguous, with opt-in meeting such requirements.(40)

Nonetheless, it should be noted that consent is not an absolute requirement for processing personal data under GDPR. Indeed, this is permitted if justified by one of six lawful bases, all equivalent to consent in importance.(40) Hence, if consent is chosen as the basis for processing of health data in Europe, such must be on an opt-in basis. However, if the justification for processing data falls under another of the six bases outlined by GDPR, processing patient data may still be lawful (for instance, using data to protect valid interests of the patient).

Thus, it is predicted that opt-out consent is to be superseded by opt-in consent for observational research in Europe. This is only applicable if there are no other lawful bases under which the data is being processed. In observational studies, researchers may consider either utilising one of the alternative bases- rather than relying on consent- or fully anonymising information, consequently abstracting it from the ambit of GDPR altogether. Any such decision will require greater scrutiny prior to acceptance as part of a research proposal.

CONCLUSIONS

Consistently with the literature available, participants in our focus group were positive about the use of opt-out consent in observational research. Participants understood opt-out consent's benefits to scientific knowledge and future generations, also appreciating its advantageousness to researchers and to participants themselves. Key concerns which emerged focussed on privacy and the use of data from opt-out research by third parties. There is also an irrefutable need for exhaustive yet accessible education and information on opt-out consent. Improving education of the public regarding opt-out consent is likely to remove the perceived barriers to this consent methodology, augmenting public trust whilst curbing misbeliefs. This, in

392 turn, could decrease selection bias in research, empowering more equitable care for all patients. A

393 potential impediment, however, is represented by the coming into force of the General Data

394 Protection Regulation in Europe.

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DISCLOSURES

No conflicts of interest to declare.

EHTICAL APPROVAL

Local audit approval was obtained for the focus group as part of ongoing work regarding opt out consent as part of standard care.

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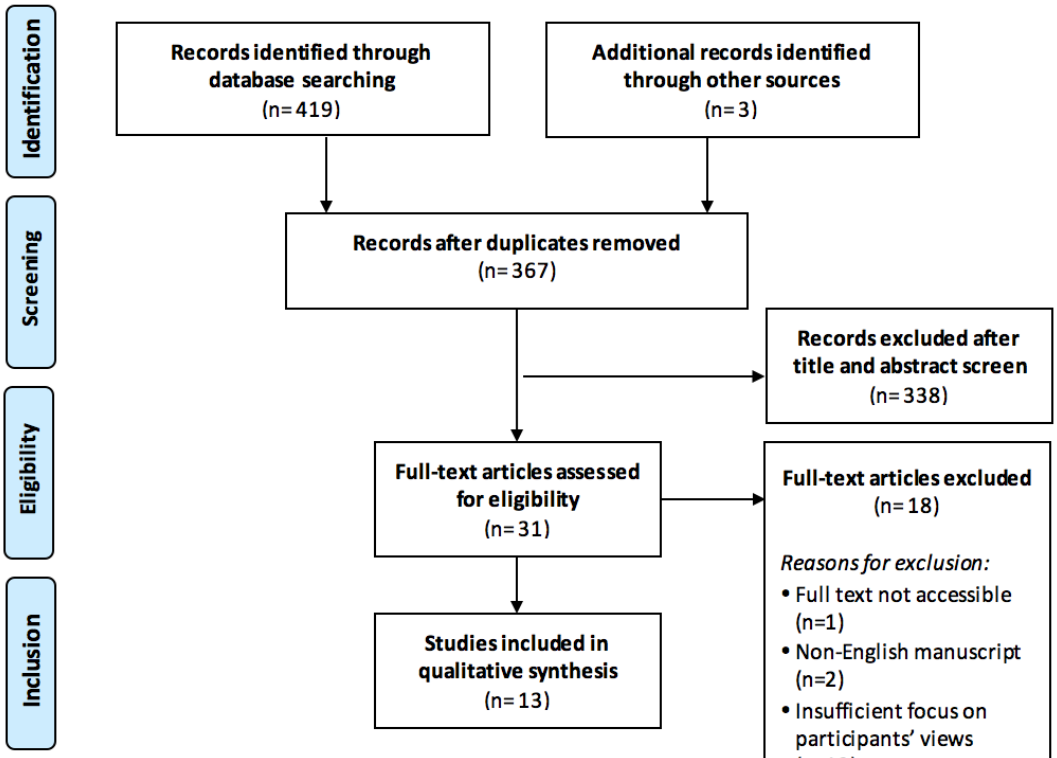
40. Regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data, and repealing Directive 95/46/EC (General Data Protection Regulation) (Text with EEA relevance), (2016).

524 **Figure 1.** PRISMA flow chart of literature review.



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527 **Table 1.** Focus group interview questions.

Part 1	
Patients' involvement and understanding of medical research	What is your understanding of medical research? Have you or someone you know ever been approached to participate in medical research? Have you/would you participate in medical research? Do you know what an “opt-out” system is?
Part 2	**Presentation on selection bias and opt-out consent**
Patients' views on opt-out consent	How would you feel if an "opt-out" system were applied to medical research? Would you participate in an “opt-out” medical study? How should we inform patients about our "opt-out" system? Who should support & counsel patients who have questions? How would you feel if your anonymized data were shared with third parties?

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530 **Table 2.** Summary of existing literature audited.

Author	Region	Method of data collection	Participants (number)
Botkin et al. (27)	USA	Focus groups	131
Brothers et al. (23)	USA	Telephonic survey	1022
Brothers et al. (22)	USA	In person survey	237
Brothers et al. (24)	USA	Semi-structured interviews	84
Damschroder et al. (28)	USA	Telephonic survey and deliberation session	513
Fernandes et al. (29)	USA	In person survey	166
Kass et al. (30)	USA	Single structured interview (telephonic/in person)	602
Lewis et al. (25)	UK	Focus groups and online survey	1181
Simon et al. (26)	USA	Focus groups and telephonic survey	799
Spencer et al. (31)	UK	Focus groups and interviews	40
Stevenson et al. (32)	UK	Focus groups and interviews	57
Taylor et al. (33)	UK	Focus groups and survey	28
Willison et al. (34)	Canada	Semi-structured interviews and structured, fixed response survey	123

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Table 3. Themes supportive of opt-out consent identified in existing literature. **Blue** cells indicate themes also identified in the focus group interview held.

Study	*Rationale for supporting opt-out research*				*Trust*	*Convenience*		*Presence of safeguards*		
	Research advances medical knowledge	**Research benefits others**	**Research benefits self/family**	**Research benefits other people with same disease**	**Trust researchers /research institution**	**Not being repeatedly asked for consent**	**More cost/ time effective**	**As long as opting-out is possible**	**As long as records are anonymous**	**As long as an independent "watchdog" exists**
(27)	✓	✓					✓	✓		✓
(23)					✓			✓	✓	
(22)	✓	✓	✓	✓	✓					
(24)		✓	✓	✓	✓					
(28)	✓				✓					
(29)	✓									
(30)	✓				✓				✓	
(25)	✓					✓	✓	✓		
(26)	✓	✓					✓			
(31)	✓				✓					
(32)	✓				✓				✓	
(33)		✓						✓		✓
(34)	✓	✓								

Table 4. Themes of concern over opt-out consent identified in existing literature. **Blue** cells indicate themes also identified in the focus group interview held.

Study	*Data protection*		*Third parties and inappropriate use of data*			*Information and ability to opt-out*			
	Concern for privacy	**Sceptical security is sufficient**	**Commercial use of data (drug companies)**	**Inappropriate use by third parties (insurances, banks)**	**Data basis for discrimination**	**Desire for more information/ explanations**	**Initial informative letter may not be read/understood**	**Difficulty in indicating will to opt-out**	**Passive form of consent**
(27)	✓			✓		✓			
(23)									
(22)	✓					✓			
(24)	✓								
(28)	✓		✓			✓			
(29)	✓					✓	✓	✓	
(30)	✓	✓			✓				
(25)									
(26)	✓			✓		✓	✓		✓
(31)	✓	✓		✓		✓			
(32)	✓		✓	✓		✓	✓		
(33)	✓	✓	✓	✓	✓	✓	✓		
(34)				✓		✓			

Table 5. Demographics of focus group participants obtained via paper survey.

	N=13
Age (%)	
Less than 30	0 (0)
30-39	1 (10)
40-49	3 (30)
50-59	1 (10)
60-69	5 (50)
70 or over	3 (30)
Self-defined ethnicity (%)	
White British	10 (77)
White Irish	2 (15)
Ashkenazi Jewish	1 (8)
Educational level (%)	
No qualifications	3 (30)
Qualifications below degree level	6 (60)
Degree or higher	4 (40)
Relation to Guy's Hospital (%)	
Patient	10 (77)
Partner	3 (23)
Family member	0 (0)
Other carer	0 (0)
If a patient, reason for attending Guy's Hospital (%)	
Medical reason other than cancer	0 (0)
At risk of developing cancer	1 (10)
Cancer diagnosis	9 (90)
Cancer type (%)	
Bladder	1 (10)
Prostate	5 (50)
Testicular	1 (10)
Breast	2 (20)
Lung	1 (10)
Employment status (%)	
Unemployed	3 (23)
Retired	6 (46)
Full-time	4 (31)
Part-time	0 (0)
Sick-leave	0 (0)
Distance from hospital (%)	
<5 miles	5 (38)
5-10 miles	2 (15)

10-15 miles	3 (23)
15+ miles	3 (23)

Table 6. Supporting quotations from focus group participants approving opt-out consenting.

Participant identifier	Quotation
Patient #9	"I'm a big believer of the opt-out system, it makes total sense to me."
Patient #1	"I definitely believe in an opt-out system."
Patient #3	"[An opt-out system] wouldn't bother me."
Patient #5	"In the principle of an opt-out system I'm in favour of."
Partner #2	"It wouldn't be a problem!"
Patient #4	"It's fine, as long as it's crystal clear you are given the opportunity to opt out."

Table 7. Representative statements supporting an opt-out consent strategy.

Rationale for supporting opt out research	
Advancing medical knowledge	I think research is [useful to] understanding what happens in the body and how diseases develop, and that in turn can be used to develop treatments. That's why I'd do it.
Benefitting future generations	[I'd participate] for my children, grandchildren, any children.
	For the next generation, that's why I'd do it.
Gratefulness to past participants	I feel very strongly that I am standing on the shoulders of other people who developed and supported research, medicine, cures up to this point. My job is to continue this.
Trust for researchers and research institutions	
Participation and trust in researchers	We have great trust in you, we do, that's why we wouldn't drop out.
Participation and care standards	*Interviewer*: Do you think you'd have a different level of care if you didn't take part in an opt-out study? *Patient #5*: No, not at all *All*: [shaking heads]
Safeguards- opportunity to opt-out	
Safeguard of clear opt-out choice	As long as it's clear you are given the opportunity to opt out, it's fine.
	If you got the option [to opt-out] and it's clear, wouldn't bother me.
Harassing research requests	
Concern for harassment resolved with opt-out	You always think you're going to get harassed, you need something to make that clear, that you're not going to be inundated with calls, emails…
	[It should be] made clear and honest that you're not going to get contacted and anything like that, even when you're in. You want to make it clear to people that staying in doesn't mean you're going to get bombarded.

Table 8. Representative statements of concerns on an opt-out consent strategy.

Data protection and privacy	
Inevitability of data corruption	I realize that there is always a risk that data is leaked. […] I think it's about trust, we live in that era… is your stuff safe? I don't suppose it's safe no matter where it is so straight away I'm on the defence.
Knowledge of safeguards to privacy	There are laws about this kind of information. […] I'm sure that none of them are perfect, but there is still value in having some guards on it. And I guess that's one thing that matters, assuming that no system is ever perfect; have we put safeguards in there? […] Part of it is how do we make sure that we know when [breaches] happen and how can we control that.
Sharing information with pharmaceutical companies	
Third parties and data	I am really happy to share information and data but I don't necessarily want drug companies to use my data, because I think they are deeply dodgy in how the deal with data.
Dilemma of sharing data with pharmaceutical companies	The problem is that pharmaceutical companies *do* genuinely do useful research, so there's a real dilemma here.
	You need a data set to say that this is a drug that is worthwhile for drug companies to make, that's why we need to give data to drug companies.
Inappropriate use of data by other third parties	
Discrimination by inappropriate data use	I think there are patient concerns around insurances, mortgages and other things, about them discriminating patients with data.
	I'd actually think that for lots of people who want to get a mortgage or a loan or health insurance this data would really need to be protected.
Patients' comprehension of opt-out consent	
Patients unable to understand opt-out paperwork	It must be very simple because people won't read it if it's a lot of text. It's going to be quite difficult to get the right balance between information and access, as they say the reading age of the UK is a 9-year-old, so a lot of patients won't be able to even understand complex texts.
	Especially for elderly patients, or patients who haven't been in the UK that long, come from a different culture: there are all sorts of reasons because people might not get it.
Clarity of information given	It's about making people understand: educating, understanding and being clear and concise about it.
Use of digital media for information	Does everyone here get a text message before their appointment? There could be a link on the bottom of that, so when you press that link on your phone it goes straight to a video.
Desire for more information	

Informing patients provides incentive to participation	There's also a story to be told like: "These are the diseases we figured how to treat through data". […] It's a story to be told, it's not just someone in a lab experimenting and sometimes getting it right… […] There's a story about it which is more than information, it's about sense-making for people: "This is why data matters, this is why you should be thoughtful about your data, and this is also why you might want to consider not opting-out."
	It's quite important: how do you keep people giving their data? Making them feel proud about what they've done.